

This listing of claims will replace all prior versions, and listings, of claims in the application. In amendments to the claims, additions are represented by underlining and deletions are represented by ~~striketrough~~.

### Listing of Claims

42. (currently amended) An *in vitro* method of cloning nucleic acid molecules, the method comprising

(a) dividing a nucleic acid sample to produce a plurality of separate amplification reactions,

(b) amplifying nucleic acid molecules in the amplification reactions by rolling circle amplification to form tandem sequence DNA,

(c) making a replica of the amplification reactions, and

(d) testing nucleic acid molecules in either the amplification reactions or the replica amplification reactions to identify nucleic acid molecules of interest~~interest~~, and

~~(e) retrieving the identified nucleic acid molecules of interest from the corresponding amplification reactions or replica amplification reactions that were not tested.~~

43. (original) The method of claim 42 wherein the nucleic acid sample is divided by spreading the sample onto a surface to form a spread, and wherein the separate amplification reactions are the locations of circular vectors on the surface after spreading.

44. (original) The method of claim 43 wherein the replica of the amplification reactions is made by contacting the spread with a second surface to which nucleic acids can bind.

45. (original) The method of claim 42 wherein the method further comprises, prior to dividing the nucleic acid sample,

diluting the nucleic acid sample such that, on average, each amplification reaction contains a single nucleic acid molecule.

53. (previously presented) The method of claim 42 further comprising~~An *in vitro* method of cloning nucleic acid molecules, the method comprising~~

~~(a) dividing a nucleic acid sample to produce a plurality of separate amplification reactions,~~

- ~~(b) amplifying nucleic acid molecules in the amplification reactions,~~
- ~~(c) making a replica of the amplification reactions,~~
- ~~(d) testing nucleic acid molecules in either the amplification reactions or the replica amplification reactions to identify nucleic acid molecules of interest, and~~
- (e) screening the identified nucleic acid molecules of interest by coupled transcription-translation to identify nucleic acid molecules encoding protein molecules with a specific catalytic activity.

Claims 54-56 (canceled).

57. (currently amended) The method of claim 42 further comprising~~An *in vitro* method of cloning nucleic acid molecules, the method comprising~~

- ~~(a) dividing a nucleic acid sample to produce a plurality of separate amplification reactions,~~
- ~~(b) amplifying nucleic acid molecules in the amplification reactions,~~
- ~~(c) making a replica of the amplification reactions,~~
- ~~(d) testing nucleic acid molecules in either the amplification reactions or the replica amplification reactions to identify nucleic acid molecules of interest, and~~
- (e) subjecting the identified nucleic acid molecules of interest to coupled transcription-translation to produce transcripts and proteins.

58. (previously presented) The method of claim 57 further comprising screening the proteins to identify those with an activity of interest.

Claims 59-61 (canceled).

62. (currently amended) The method of claim 42 wherein the nucleic acid molecules are amplified by~~A method of isolating and amplifying nucleic acid molecules, the method comprising~~

- (a) inserting a plurality of nucleic acid molecules into a plurality of linear vectors in a single reaction to form a plurality of circular vectors, each circular vector comprising a vector and a nucleic acid molecule,

wherein the linear vectors are double-stranded linear nucleic acid comprising two nucleic acid strands, wherein the circular vectors each contain at least one nick, gap, or overlap in the second strand, and wherein the first strand in each circular vector is a closed circular strand,

(b) separating the first strands from the second strands,

(c) diluting and dividing the first strands to produce a plurality of separate amplification reactions that, on average, each contain a single circular vector,

(d) amplifying the first strands of the plurality of circular vectors by rolling circle replication to form tandem sequence DNA,

wherein the amplification results in amplification of the nucleic acid molecules in the first strands.

63. (currently amended) The method of claim 42~~claim 62~~ wherein the tandem sequence DNA is amplified by strand displacement replication to form secondary tandem sequence DNA.

64. (previously presented) The method of claim 63 wherein the secondary tandem sequence DNA is amplified by strand displacement replication to form tertiary tandem sequence DNA.

65. (currently amended) The method of claim 42 wherein the nucleic acid molecules are amplified by~~A method of isolating and amplifying a nucleic acid molecule, the method comprising~~

(a) inserting a nucleic acid molecule into a linear vector to form a circular vector comprising the vector and the nucleic acid molecule,

wherein the linear vector is a double-stranded linear nucleic acid comprising two nucleic acid strands, wherein the circular vector contains at least one nick in the second strand and wherein the first strand in the circular vector is a closed circular strand,

(b) amplifying the first strand,

wherein the amplification results in amplification of the nucleic acid molecule in the first strand.

66. (currently amended) The method of claim 42 wherein the nucleic acid molecules are amplified by~~A method of isolating and amplifying nucleic acid molecules, the method comprising~~

(a) forming a plurality of circular vectors, wherein each circular vector comprises a nucleic acid molecule,

wherein the vectors are double-stranded nucleic acid comprising two nucleic acid strands, wherein the circular vectors each contain at least one nick, gap, or overlap in the second strand, and wherein the first strand in each circular vector is a closed circular strand,

(b) separating the first strands from the second strands,

(c) diluting and dividing the first strands to produce a plurality of separate amplification reactions that, on average, each contain a single circular vector,

(d) amplifying the first strands of the plurality of circular vectors by rolling circle replication to form tandem sequence DNA,

wherein the amplification results in amplification of the nucleic acid molecules in the first strands.

Claim 67 (canceled).

Claim 68 (canceled).

69. (currently amended) The method of claim 42 wherein the nucleic acid molecules are amplified by~~A method of isolating and amplifying a nucleic acid molecule, the method comprising~~

(a) forming a circular vector comprising a nucleic acid molecule,

wherein the vector is a double-stranded nucleic acid comprising two nucleic acid strands, wherein the circular vector contains at least one nick in the second strand and wherein the first strand in the circular vector is a closed circular strand,

(b) amplifying the first strand,

wherein the amplification results in amplification of the nucleic acid molecule in the first strand.

70. (currently amended) A kit for use in rolling circle amplification to isolate and amplify~~isolating and amplifying~~ nucleic acid molecules, the kit comprising

(a) a linear vector wherein the linear vector is a double-stranded linear nucleic acid comprising two nucleic acid strands, and wherein the linear vector contains at least one nick, wherein the nick cannot be ligated,

(b) a rolling circle replication primer, wherein the rolling circle replication primer is complementary to a portion of the first strand of the linear vector; and

(c) a strand displacement primer, wherein the strand displacement primer matches a portion of the first strand of the linear vector.

71. (currently amended) A kit for use in rolling circle amplification to isolate and amplify~~isolating and amplifying~~ nucleic acid molecules, the kit comprising

(a) a linear vector wherein the linear vector is a double-stranded linear nucleic acid comprising two nucleic acid strands, and wherein either the 5' or the 3' end of the second strand of the linear vector cannot be ligated,

(b) a rolling circle replication primer, wherein the rolling circle replication primer is complementary to a portion of the first strand of the linear vector; and

(c) a strand displacement primer, wherein the strand displacement primer matches a portion of the first strand of the linear vector.

72. (currently amended) A kit for use in rolling circle amplification to isolate and amplify~~isolating and amplifying~~ nucleic acid molecules, the kit comprising

(a) a linear vector wherein the linear vector is a double-stranded linear nucleic acid comprising two nucleic acid strands, and wherein the second strand of the linear vector contains at least one gap,

(b) a rolling circle replication primer, wherein the rolling circle replication primer is complementary to a portion of the first strand of the linear vector; and

(c) a strand displacement primer, wherein the strand displacement primer matches a portion of the first strand of the linear vector.

73. (currently amended) A kit for use in rolling circle amplification to isolate and amplify~~isolating and amplifying~~ nucleic acid molecules, the kit comprising

(a) a linear vector wherein the linear vector is a double-stranded linear nucleic acid comprising two nucleic acid strands, and wherein the second strand of the linear vector contains at least one overlap, or

(b) a rolling circle replication primer, wherein the rolling circle replication primer is complementary to a portion of the first strand of the linear vector; and

(c) a strand displacement primer, wherein the strand displacement primer matches a portion of the first strand of the linear vector.

74. (currently amended) A linear vector for use in rolling circle amplification wherein the linear vector is a double-stranded linear nucleic acid comprising two nucleic acid strands, wherein the second strand of the linear vector contains an affinity tag, and wherein the linear vector contains at least one nick, wherein the nick cannot be ligated.

75. (currently amended) A linear vector for use in rolling circle amplification wherein the linear vector is a double-stranded linear nucleic acid comprising two nucleic acid strands, wherein the second strand of the linear vector contains an affinity tag, and wherein either the 5' or the 3' end of the second strand of the linear vector cannot be ligated.

76. (currently amended) A linear vector for use in rolling circle amplification wherein the linear vector is a double-stranded linear nucleic acid comprising two nucleic acid strands, wherein the second strand of the linear vector contains an affinity tag, and wherein the second strand of the linear vector contains at least one gap.

77. (currently amended) A linear vector for use in rolling circle amplification wherein the linear vector is a double-stranded linear nucleic acid comprising two nucleic acid strands, wherein the second strand of the linear vector contains an affinity tag, and wherein the second strand of the linear vector contains at least one overlap.

78. (previously presented) A method of isolating and amplifying a nucleic acid molecule, the method comprising

(a) coupling a nucleic acid molecule to a linear vector to form a circular vector comprising the vector and the nucleic acid molecule,

wherein the linear vector is a double-stranded linear nucleic acid comprising two nucleic acid strands, wherein the second strand of the circular vector is discontinuous, and wherein the first strand in the circular vector is a closed circular strand,

(b) amplifying the first strand by rolling circle replication to form tandem sequence DNA,

wherein the amplification results in amplification of the nucleic acid molecule in the first strand,

wherein the second strand of the linear vector contains at least one nick, wherein the nick cannot be coupled.

79. (previously presented) A method of isolating and amplifying a nucleic acid molecule, the method comprising

(a) coupling a nucleic acid molecule to a linear vector to form a circular vector comprising the vector and the nucleic acid molecule,

wherein the linear vector is a double-stranded linear nucleic acid comprising two nucleic acid strands, wherein the second strand of the circular vector is discontinuous, and wherein the first strand in the circular vector is a closed circular strand,

(b) amplifying the first strand by rolling circle replication to form tandem sequence DNA,

wherein the amplification results in amplification of the nucleic acid molecule in the first strand,

wherein either the 5' or the 3' end of the second strand of the linear vector cannot be coupled.

80. (previously presented) A method of isolating and amplifying a nucleic acid molecule, the method comprising

(a) inserting a nucleic acid molecule into a linear vector to form a circular vector comprising the vector and the nucleic acid molecule,

wherein the linear vector is a double-stranded linear nucleic acid comprising two nucleic acid strands, wherein the second strand of the circular vector is discontinuous, and wherein the first strand in the circular vector is a closed circular strand,

(b) amplifying the first strand by rolling circle replication to form tandem sequence DNA,

wherein the amplification results in amplification of the nucleic acid molecule in the first strand.

81. (previously presented) The method of claim 80 wherein the second strand of the linear vector contains at least one nick, wherein the nick cannot be ligated.

82. (previously presented) The method of claim 80 wherein either the 5' or the 3' end of the second strand of the linear vector cannot be ligated.

83. (previously presented) The method of claim 80 wherein the second strand of the linear vector contains at least one gap or overlap.

84. (previously presented) The method of claim 80 wherein the method further comprises, following insertion and prior to amplification, separating the first strand from the second strand.

85. (previously presented) The method of claim 84 wherein the second strand includes an affinity tag.

86. (previously presented) The method of claim 85 wherein the first strand is separated from the second strand by binding the affinity tag to a substrate, denaturing the first and second strands prior to, simultaneous with, or following binding, and separating the first strand from the substrate.

87. (previously presented) The method of claim 84 wherein the second strand of the linear vector contains at least one overlap, part of the overlapping portions of the second strand are complementary, and the 3' end of the overlap extends beyond the part of the overlapping portions that are complementary,

wherein the first strand is separated from the second strand by ligating one end of the second strand to a nucleic acid molecule coupled to a substrate, denaturing the first and second strands following ligation of the second strand, and separating the first strand from the substrate.

88. (previously presented) The method of claim 80 wherein step (a) comprises inserting a plurality of nucleic acid molecules into a plurality of linear vectors in a single reaction to form a plurality of circular vectors, each circular vector containing at least one nick, gap, or overlap in the second strand,

wherein step (b) comprises amplifying the first strand of the plurality of circular vectors, and

wherein the method further comprises, prior to amplification, dividing the insertion reaction to produce a plurality of separate amplification reactions.



89. (previously presented) The method of claim 88 further comprising making a replica of the amplification reactions.

90. (previously presented) The method of claim 89 wherein the replica of the amplification reactions is made by contacting the amplification reactions with a surface to which nucleic acids can bind.

91. (previously presented) The method of claim 89 wherein the replica of the amplification reactions is made by transferring part of each amplification reaction to form a replica amplification reaction.

92. (previously presented) The method of claim 88 wherein the insertion reaction is divided by spreading the insertion reaction onto a surface to form a spread, and wherein the separate amplification reactions are the locations of circular vectors on the surface after spreading.

93. (previously presented) The method of claim 92 further comprising making a replica of the amplification reactions.

94. (previously presented) The method of claim 93 wherein the replica is made by contacting the spread with a second surface to which nucleic acids can bind.

95. (previously presented) The method of claim 88 wherein any number or all of the amplification reactions are ordered as an array of reaction droplets or in an array of reaction vessels.

96. (previously presented) The method of claim 95 wherein, following amplification, all or part of the contents of any number or all the individual reaction droplets or reaction vessels are transferred by one to one mapping to a new set of reaction droplets or reaction vessels.

97. (previously presented) The method of claim 96 further comprising, following amplification,

determining the presence of amplified nucleic acid in the amplification reactions, and  
transferring all or a part of the contents of the amplification reactions containing amplified nucleic acid reaction to a new set of reaction droplets or reaction vessels.

98. (previously presented) The method of claim 95 further comprising making a replica of the amplification reactions.

99. (previously presented) The method of claim 98 wherein the replica of the amplification reactions is made by contacting the amplification reactions with a surface to which nucleic acids can bind.

100. (previously presented) The method of claim 98 wherein the replica of the amplification reactions is made by contacting the amplification reactions with a surface treated with an affinity target capable of binding an affinity tag, wherein the amplified nucleic comprises affinity tags incorporated during amplification,

wherein a portion of each amplification reaction is transferred to the surface.

101. (previously presented) The method of claim 100 wherein the affinity tag is biotin and the affinity target is streptavidin.

102. (previously presented) The method of claim 100 wherein the affinity tag is a reactive moiety and the affinity target is a corresponding reactive moiety, where a chemical reaction between the affinity tag and the affinity target results in the amplified nucleic acid being covalently coupled to the surface.

103. (previously presented) The method of claim 102 wherein the affinity target is phenylene diisothiocyanate, disuccinimidylcarbonate, disuccinimidylloxolate or dimethylsuberimide and the affinity tag is a reactive amine.

104. (previously presented) The method of claim 98 wherein the replica of the amplification reactions is made by transferring part of each amplification reaction to form a replica amplification reaction.

105. (previously presented) The method of claim 95 wherein, following amplification, all or part of the contents of any number or all of the reaction droplets or reaction vessels are transferred and combined to create one or more sets of pooled reactions.

106. (previously presented) The method of claim 95 wherein the amplification reactions are arranged on the surface of a substrate.

107. (previously presented) The method of claim 106 wherein the substrate comprises acrylamide, cellulose, nitrocellulose, polystyrene, polyethylene vinyl acetate, polypropylene, polymethacrylate, polyethylene, polyethylene oxide, glass, polysilicates, polycarbonates, teflon, fluorocarbons, nylon, silicon rubber, polyanhydrides, polyglycolic acid, polylactic acid,

polyorthoesters, polypropylfumerate, collagen, glycosaminoglycans, polyamino acids, chemical resistant metals, or corrosion resistant metals.

108. (previously presented) The method of claim 88 wherein the method further comprises, prior to dividing the insertion reaction,

diluting the insertion reaction such that, on average, each amplification reaction contains a single circular vector.

109. (previously presented) The method of claim 88 wherein the method further comprises, following amplification, collecting a sample of each amplification reaction.

110. (previously presented) The method of claim 88 wherein the method further comprises detecting or sequencing the nucleic acid molecules in the amplification reactions or in the collected samples.

111. (previously presented) The method of claim 80 wherein rolling circle replication is primed by the second strand.

112. (previously presented) The method of claim 80 wherein rolling circle replication is primed by a rolling circle replication primer.

113. (previously presented) The method of claim 112 wherein the tandem sequence DNA is amplified by strand displacement replication to form secondary tandem sequence DNA.

114. (previously presented) The method of claim 113 wherein the secondary tandem sequence DNA is amplified by strand displacement replication to form tertiary tandem sequence DNA.

115. (previously presented) The method of claim 113 wherein strand displacement replication of the tandem sequence is primed by a strand displacement primer.

116. (previously presented) The method of claim 88 further comprising detecting one or more amplified nucleic acid molecules in one or more of the amplification reactions.

117. (previously presented) The method of claim 116 wherein the nucleic acid molecules are derived from cDNA generated by suppression subtractive hybridization.

118. (previously presented) The method of claim 116 wherein the plurality of nucleic acid molecules are all derived from the same source.

119. (previously presented) The method of claim 116 further comprising, following amplification,

creating a replica of the amplification reactions,  
contacting the amplification reactions with a first set of labeled nucleic acid probes and the replica amplification reactions with a second set of labeled nucleic acid probes, and  
comparing the pattern of hybridization of the first set of probes to the pattern of hybridization of the second set of probes,

wherein differences in the patterns of hybridization indicate differences in the probe sets.

120. (previously presented) The method of claim 119 further comprising  
selecting for isolation or further analysis amplification reactions that hybridize to the first set of probes but not to the second set of probes, amplification reactions that hybridize to the second set of probes but not to the first set of probes, amplification reactions that hybridize to the both sets of probes, or amplification reactions that do not hybridize to either set of probes.

121. (previously presented) A method of isolating and amplifying a nucleic acid molecule, the method comprising

(a) forming a circular vector comprising a nucleic acid molecule,  
wherein the vector is a double-stranded nucleic acid comprising two nucleic acid strands, wherein the second strand of the circular vector is discontinuous, and wherein the first strand in the circular vector is a closed circular strand,

(b) amplifying the first strand by rolling circle replication to form tandem sequence DNA,

wherein the amplification results in amplification of the nucleic acid molecule in the first strand.

122. (previously presented) The method of claim 121 wherein the second strand of the linear vector contains at least one nick, wherein the nick cannot be ligated.

123. (previously presented) The method of claim 121 wherein either the 5' or the 3' end of the second strand of the linear vector cannot be ligated.

124. (previously presented) The method of claim 121 wherein the second strand of the linear vector contains at least one gap or overlap.

125. (previously presented) The method of claim 121 wherein the method further comprises, following formation and prior to amplification, separating the first strand from the second strand.

126. (previously presented) The method of claim 125 wherein the second strand includes an affinity tag.

127. (previously presented) The method of claim 126 wherein the first strand is separated from the second strand by binding the affinity tag to a substrate, denaturing the first and second strands prior to, simultaneous with, or following binding, and separating the first strand from the substrate.

128. (previously presented) The method of claim 125 wherein the second strand of the linear vector contains at least one overlap, part of the overlapping portions of the second strand are complementary, and the 3' end of the overlap extends beyond the part of the overlapping portions that are complementary,

wherein the first strand is separated from the second strand by ligating one end of the second strand to a nucleic acid molecule coupled to a substrate, denaturing the first and second strands following ligation of the second strand, and separating the first strand from the substrate.

129. (previously presented) The method of claim 121 wherein step (a) comprises forming a plurality of circular vectors, each circular vector comprising a nucleic acid molecule, and each circular vector containing at least one nick, gap, or overlap in the second strand, wherein step (b) comprises amplifying the first strand of the plurality of circular vectors, and

wherein the method further comprises, prior to amplification, dividing the formation reaction to produce a plurality of separate amplification reactions.

130. (previously presented) The method of claim 129 further comprising making a replica of the amplification reactions.

131. (previously presented) The method of claim 130 wherein the replica of the amplification reactions is made by contacting the amplification reactions with a surface to which nucleic acids can bind.

132. (previously presented) The method of claim 130 wherein the replica of the amplification reactions is made by transferring part of each amplification reaction to form a replica amplification reaction.

133. (previously presented) The method of claim 129 wherein the formation reaction is divided by spreading the formation reaction onto a surface to form a spread, and wherein the separate amplification reactions are the locations of circular vectors on the surface after spreading.

134. (previously presented) The method of claim 133 further comprising making a replica of the amplification reactions.

135. (previously presented) The method of claim 134 wherein the replica is made by contacting the spread with a second surface to which nucleic acids can bind.

136. (previously presented) The method of claim 129 wherein any number or all of the amplification reactions are ordered as an array of reaction droplets or in an array of reaction vessels.

137. (previously presented) The method of claim 136 wherein, following amplification, all or part of the contents of any number or all the individual reaction droplets or reaction vessels are transferred by one to one mapping to a new set of reaction droplets or reaction vessels.

138. (previously presented) The method of claim 137 further comprising, following amplification,

determining the presence of amplified nucleic acid in the amplification reactions, and transferring all or a part of the contents of the amplification reactions containing amplified nucleic acid reaction to a new set of reaction droplets or reaction vessels.

139. (previously presented) The method of claim 136 further comprising making a replica of the amplification reactions.

140. (previously presented) The method of claim 139 wherein the replica of the amplification reactions is made by contacting the amplification reactions with a surface to which nucleic acids can bind.

141. (previously presented) The method of claim 139 wherein the replica of the amplification reactions is made by contacting the amplification reactions with a surface treated

with an affinity target capable of binding an affinity tag, wherein the amplified nucleic comprises affinity tags incorporated during amplification,

wherein a portion of each amplification reaction is transferred to the surface.

142. (previously presented) The method of claim 141 wherein the affinity tag is biotin and the affinity target is streptavidin.

143. (previously presented) The method of claim 141 wherein the affinity tag is a reactive moiety and the affinity target is a corresponding reactive moiety, where a chemical reaction between the affinity tag and the affinity target results in the amplified nucleic acid being covalently coupled to the surface.

144. (previously presented) The method of claim 143 wherein the affinity target is phenylene diisothiocyanate, disuccinimidylcarbonate, disuccinimidylxolate or dimethylsuberimide and the affinity tag is a reactive amine.

145. (previously presented) The method of claim 139 wherein the replica of the amplification reactions is made by transferring part of each amplification reaction to form a replica amplification reaction.

146. (previously presented) The method of claim 136 wherein, following amplification, all or part of the contents of any number or all of the reaction droplets or reaction vessels are transferred and combined to create one or more sets of pooled reactions.

147. (previously presented) The method of claim 136 wherein the amplification reactions are arranged on the surface of a substrate.

148. (previously presented) The method of claim 147 wherein the substrate comprises acrylamide, cellulose, nitrocellulose, polystyrene, polyethylene vinyl acetate, polypropylene, polymethacrylate, polyethylene, polyethylene oxide, glass, polysilicates, polycarbonates, teflon, fluorocarbons, nylon, silicon rubber, polyanhydrides, polyglycolic acid, polylactic acid, polyorthoesters, polypropylfumerate, collagen, glycosaminoglycans, polyamino acids, chemical resistant metals, or corrosion resistant metals.

149. (previously presented) The method of claim 129 wherein the method further comprises, prior to dividing the formation reaction,

diluting the formation reaction such that, on average, each amplification reaction contains a single circular vector.

150. (previously presented) The method of claim 129 wherein the method further comprises, following amplification, collecting a sample of each amplification reaction.

151. (previously presented) The method of claim 129 wherein the method further comprises detecting or sequencing the nucleic acid molecules in the amplification reactions or in the collected samples.

152. (previously presented) The method of claim 121 wherein rolling circle replication is primed by the second strand.

153. (previously presented) The method of claim 121 wherein rolling circle replication is primed by a rolling circle replication primer.

154. (previously presented) The method of claim 153 wherein the tandem sequence DNA is amplified by strand displacement replication to form secondary tandem sequence DNA.

155. (previously presented) The method of claim 154 wherein the secondary tandem sequence DNA is amplified by strand displacement replication to form tertiary tandem sequence DNA.

156. (previously presented) The method of claim 154 wherein strand displacement replication of the tandem sequence is primed by a strand displacement primer.

157. (previously presented) The method of claim 129 further comprising detecting one or more amplified nucleic acid molecules in one or more of the amplification reactions.

158. (previously presented) The method of claim 157 wherein the nucleic acid molecules are derived from cDNA generated by suppression subtractive hybridization.

159. (previously presented) The method of claim 157 wherein the plurality of nucleic acid molecules are all derived from the same source.

160. (previously presented) The method of claim 157 further comprising, following amplification,

creating a replica of the amplification reactions,

contacting the amplification reactions with a first set of labeled nucleic acid probes and the replica amplification reactions with a second set of labeled nucleic acid probes, and



comparing the pattern of hybridization of the first set of probes to the pattern of hybridization of the second set of probes,

wherein differences in the patterns of hybridization indicate differences in the probe sets.

161. (previously presented) The method of claim 160 further comprising selecting for isolation or further analysis amplification reactions that hybridize to the first set of probes but not to the second set of probes, amplification reactions that hybridize to the second set of probes but not to the first set of probes, amplification reactions that hybridize to the both sets of probes, or amplification reactions that do not hybridize to either set of probes.

162. (currently amended) An *in vitro* method of cloning nucleic acid molecules, the method comprising

(a) dividing a nucleic acid sample to produce a plurality of separate amplification reactions,

(b) amplifying nucleic acid molecules in the amplification reactions by rolling circle amplification to form tandem sequence DNA,

(c) making a replica of the amplification reactions,

(d) testing nucleic acid molecules in either the amplification reactions or the replica amplification reactions to identify nucleic acid molecules of interest by subjecting the nucleic acid molecules to coupled transcription-translation to produce transcripts and proteins, and

(e) retrieving the identified nucleic acid molecules of interest from the corresponding amplification reactions or replica amplification reactions that were not tested.

163. (previously presented) The method of claim 162 further comprising screening the proteins to identify those with an activity of interest.

164. (previously presented) The method of claim 162 wherein the nucleic acid sample is divided by spreading the sample onto a surface to form a spread, and wherein the separate amplification reactions are the locations of circular vectors on the surface after spreading.

165. (previously presented) The method of claim 163 wherein the replica of the amplification reactions is made by contacting the spread with a second surface to which nucleic acids can bind.

166. (previously presented) The method of claim 162 wherein the method further comprises, prior to dividing the nucleic acid sample,

diluting the nucleic acid sample such that, on average, each amplification reaction contains a single nucleic acid molecule.

167. (currently amended) An *in vitro* method of cloning nucleic acid molecules, the method comprising

(a) dividing a nucleic acid sample to produce a plurality of separate amplification reactions,

(b) amplifying nucleic acid molecules in the amplification reactions by rolling circle amplification to form tandem sequence DNA,

(c) making a replica of the amplification reactions,

(d) testing nucleic acid molecules in either the amplification reactions or the replica amplification reactions to identify nucleic acid molecules of interest by subjecting the nucleic acid molecules to coupled transcription-translation to produce transcripts and proteins.

168. (previously presented) The method of claim 167 further comprising screening the proteins to identify those with an activity of interest.

169. (previously presented) The method of claim 167 wherein the nucleic acid sample is divided by spreading the sample onto a surface to form a spread, and wherein the separate amplification reactions are the locations of circular vectors on the surface after spreading.

170. (previously presented) The method of claim 169 wherein the replica of the amplification reactions is made by contacting the spread with a second surface to which nucleic acids can bind.

171. (previously presented) The method of claim 167 wherein the method further comprises, prior to dividing the nucleic acid sample,

diluting the nucleic acid sample such that, on average, each amplification reaction contains a single nucleic acid molecule.

172. (new) The method of claim 42 further comprising

(e) retrieving the identified nucleic acid molecules of interest from the corresponding amplification reactions or replica amplification reactions that were not tested.